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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/014,716	12/14/2001	Stephen P.A. Fodor	018547-048200US	1441

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EXAMINER

PONNALURI, PADMASHRI

ART UNIT

PAPER NUMBER

1639

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
10/014,716

Applicant(s)
Fodor et al

Examiner
Padmashri Ponnaluri

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Jul 16, 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8-22 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 7 6) ☐ Other:

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DETAILED ACTION

1. This application is a continuation of application serial number 08/348,471, which is a continuation of application 07/805,727, which is a continuation in part of application serial number 07/492,462, which is a continuation in part of application serial number 07/624,120, which is a continuation in part of application serial number 07/492,462 and which is a continuation in part of application serial number 07/362,901.
2. Applicants are requested to update the status of parent application data in the specification page 1.
3. The preliminary amendment A, filed on 12/14/01 has been fully considered and entered into the application.
4. Claims 1-7 have been canceled by the amendment A, and new claims 8-22 have been added by the amendment A, filed on 12/14/01.
5. Claims 8-22 are currently being examined in this application.
6. The title of the application has been changed by the amendment A, filed on 12/14/01.
7. The substituted specification along with the originally specification has been entered into the application.
8. This application has been filed with informal drawings which are acceptable for examination purposes only. Formal drawings will be required when the application is allowed.

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If applicant intends to renumber the informal figures, applicant is encouraged to amend the specification so that the description of the renumbered figures corresponds to the renumbered figures.

9. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 8, 15, 18, 21-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite an apparatus comprising a body having a sealed less than 1000 μm deep cavity, and a surface comprising polymers.

The specification description is directed to a bioreactor which is used in the synthesis of either oligonucleotide or peptides, which clearly do not provide an adequate representation regarding the open ended claimed apparatus in which any polymer is attached or linked to the substrate of the apparatus as the present claimed invention. **The specification disclosure is**

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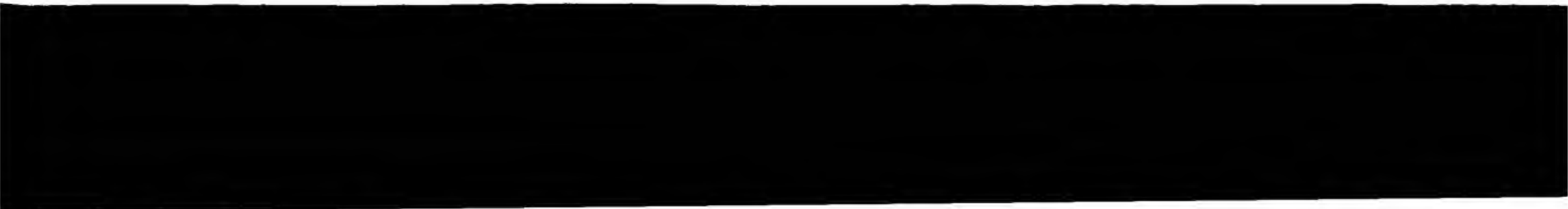
specific to the synthesis of oligonucleotide or polypeptide arrays on a solid support using photolithographic techniques. The specification does not teach an apparatus which has a 1000 μm deep cavity and a solid substrate to which polymers are linked.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any product; which requires a representative sample of compounds and a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

In the instant claimed apparatus, does not specifically teach how the polymers are linked or attached to the surface of the solid support. At the time the invention was made methods of making polymers, i.e., carbohydrates or lipids or other complex polymers was not known.

Additionally, the narrow scope of examples directed to the synthesis of specific oligonucleotides or peptides are clearly not representative of the scope of the apparatus of the presently claimed invention.



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12. Claims 8, 15, 18, 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an apparatus with oligonucleotide or peptides linked to a solid substrate, does not reasonably provide enablement for an apparatus with any other polymers linked or attached to the solid substrate. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims briefly recite an apparatus comprising a body having a sealed less than 1000 μm deep cavity, and a surface comprising polymers.

The specification discloses a reactor or an apparatus for synthesis of oligonucleotides or polypeptides and methods of using to synthesize peptides or oligonucleotides using photo labile protecting groups. The specification discloses in page 65 that the monomer reacts with its carboxyl terminus with amino groups on the regions of the substrate which have been deprotected. The specification disclosure is insufficient to enable one skilled in the art to practice the invention without an undue amount of experimentation.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (U. S. P. Q. 2d 1400; CAFC 1988) which include: the quantity of experimentation necessary; . the amount of direction or guidance presented; the presence or absence of working examples; . the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

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A number of factors would prevent one of ordinary skill in the art from practicing (making and using) the invention without undue experimentation, which are summarized as follows:

- a. The specification fails to give adequate direction and guidance as to the means of linking or attaching polymers to the solid support with the cavity of 1000 μm deep. The specification does not teach the linkage of the polymers to the solid support. The linking of the polymers to the solid substrates is unique to the polymers and the substrate used. The specification does not give guidance on how to link different polymers to the solid support or the solid supports or substrates to which the polymers linked are derivitized with any specific functional groups, such that the polymers can be linked or attached the solid supports. The specification disclosure is based on the photolithographic technique of polymer synthesis, (i.e., peptides and oligonucleotides) on a solid support. At the time the invention was made it was not routine or well known to a person skilled in the art to link or synthesize polymers such as carbohydrates to a solid support which is present in a cavity less than 1000 μm deep.
- b. The working examples are directed to the use of an apparatus in the synthesis of oligonucleotides or polypeptides on a solid support.
- c. The breadth of the claims are open-ended regarding the linkage or attachment of the polymers other than oligonucleotides and polypeptides to a support which has less than 1000 μm deep cavity, and the reaction conditions, and the order of the deprotection reactions.
- d. The art is inherently unpredictable because the linking or attaching of polymers to a solid support which is in a cavity less than 1000 μm deep is unique to the polymers linked, and without

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prior knowledge of the linkers or attachment of the polymers , it would require trials and errors to prepare such an apparatus.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 8-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 8, 11, 13 recite ‘..less than about 1000 μm deep...’ or in claims 12 and 14 recite ‘... less than about 500 μm deep...’ the metes and bounds of the terms ‘less than about’ is not known. Does applicants mean that the cavity is less than 1000 μm deep or about 1000 μm . Because if the cavity is about 1000 μm deep, any cavities more than 1000 μm deep (which is 1000 μm or above 1000 μm or less than 1000 μm) would read on the instant claims. And if the cavity is less than 1000 μm deep, any cavities less than 1000 μm deep (which includes 1 μm to 999 μm) would read. Does it is not clear what does applicants mean by less than about 1000 μm deep. Applicants are requested to amend the claim.

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15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 8-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 4,517,338 (Urdea et al) .

Urdea et al recite a reactor system for the sequential modification of a linear polymeric molecule attached to a dispersed solid-phase support, which is retained within a reactor zone for the introduction and removal of reagents (see column 3, lines 1-11). The reference teaches that the reactor system comprises one or more reactor zones which are connected to a reagent manifold capable of selectively delivering the reagents necessary for a particular reaction to each reactor zone (refers the apparatus with sealed cavity of the instant claims). The reactor zones each include at least two access ports (refers to inlet port and out let port of the instant claims) (see



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column 4, lines 34-44). The reactor zone comprises an elongated tube or column (refers to a body having a sealed body cavity of the instant claims) which is open at each end (see column 4, lines 49-50). The reactor column is a glass tube having a volume of 300 μ l (see column 5, lines 5-8). The reactor column is enclosed at either end by porous barrier, such as glass, Teflon, or stainless steel frits, the pores in the barriers are fine to retain the solid phase supports within the reactor (see column 5, lines 6-8). The solid phase support of the reactor can be controlled pore glass (see column 5, lines 20-37, in particular). The solid phase supports are in the cavity of the reactor (refers to a substrate surface contacts the cavity of the instant claims). The reference also teaches that the reactor column is loaded with a suitable solid phase support. The reference teaches that the solid support are derivitized by coupling deoxynucleoside 3'-O-succinic acid derivatives. The solid phase supports have previously derivitized with a desirable nucleoside (see column 8, lines 55-57). Urdea et al teach that the disclosed reactor system is applicable to a wide variety of chemical synthesis and degradation techniques which result in modification of a linear polymeric molecule attached to a solid phase support or support and in particular the reactor system will find use in step wise formation or degradation of linear polymeric materials, such as proteins (poly amino acids), polynucleotide or derivatives thereof (see column 3, lines 66 through column 4, lines 3). Urdea et al teach that the reactor system is applicable to a wide variety of chemical synthesis and degradation techniques which result in modification of a linear polymeric molecule attached to a solid phase support or supports and in particular the reactor

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system will find use in step wise formation or degradation of linear polymeric materials, such as proteins (poly amino acids), polynucleotide or derivatives thereof.

The claimed invention further differs from the prior art teachings only by the recitation of depth of the cavity and substrate seals the cavity. However, the solid phase supports of the reference are small porous beads and the solid phase supports are loosely packed in the column. The reference teaches that the reactor column is enclosed with at either end by barriers with pores. The pores of the barrier are fine to retain the solid phase supports within the cavity. Thus, the solid phase support surface is in contact with the body of the column, and the solid phase supports indirectly seal the cavity (the solid phase supports in the barriers). Urdea et al teach that the reactor will have a minimum volume to reduce the usage of the reagents and the dimensions of the reactor are not critical. Thus, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to use the apparatus taught by Urdea et al to obtain an apparatus with the specific dimensions, less than about 1000 μm deep cavity, with the expectation of that the in a smaller reactor the reagents volume can also be reduced. Thus, it would have been obvious to one skilled in the art at the time the invention was made to make or use a reactor taught by Urdea et al for attaching or linking polymers to support which is in a cavity of less than about 1000 μm deep.

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

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harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 U. S. P. Q. 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 U. S. P. Q. 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 U. S. P. Q. 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 U. S. P. Q. 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

18. Claims 8-22 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 6,420,169. Although the conflicting claims are not identical, they are not patentably distinct from each other because the reference claims are drawn to exactly same apparatus which is used in forming or synthesizing oligonucleotides or polypeptides and once the synthesis is complete before the polymers are removed from the solid substrate the reference apparatus would read on the instant claimed apparatus. Thus the apparatus of the instant claims is obvious over the reference apparatus.

19. No claims are allowed.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on *Increased Flex Schedule* and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
09 March 2003


PADMAASHRI PONNALURI
PRIMARY EXAMINER